#15

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Michael E. Moseley et al.	Examiner: J. Lin
Serial No.:	09/606,137	Group Art Unit: 3737
Filed:	June 28, 2000	Docket: 500.003US1
Title:	**IMAGING METHODS FOR VISUALIZING IMPLANTED LIVING CELLS**	

APPEAL BRIEF TO THE BOARD OF PATENT APPEALS AND INTERFERENCES OF THE UNITED STATES PATENT AND TRADEMARK OFFICE

MAIL STOP: APPEAL BRIEF - PATENTS
P.O. BOX 1450
Commissioner for Patents
Alexandria, VA22313-1450

Sir:

This is an appeal from the Office Action mailed on March 25, 2003 finally rejecting claims 1-43 and 47-52, all of the claims in the Application. All other claims are withdrawn/cancelled as drawn to a non-elected invention.

This Brief is being filed in triplicate along with authorization to debit **$160.00** to Deposit Account No. 50-1391 to cover the fee for the appeal for a Small Entity. Appellants request the opportunity for a personal appearance before the Board of Appeals to argue the issues of this appeal. The fee for the personal appearance will be timely paid upon receipt of the Examiner's Answer.

CERTIFICATE UNDER 37 C.F.R. 1.8: The undersigned hereby certifies that this Transmittal Letter and the paper, as described herein, are being deposited in the United States Postal Service, as first class mail, with sufficient postage, in an envelope addressed to: MAIL STOP: APPEAL BRIEFS – PATENT, P.O. BOX 1450, Commissioner for Patents, Alexandria, VA 22313-1450 September 25, 2003.

Mark A. Litman
Name

Signature

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REAL PARTY IN INTEREST

The real part of interest in this Appeal is the Regents of the University of Minnesota and their exclusive licensee for this technology, Bresagen, Inc. a small entity corporation of Australia.

RELATED APPEALS AND INTERFERENCES

Appellants do not know of any other pending U.S. Patent Applications that are on appeal which have issues that overlap with the issues in this Appeal. No Interference proceedings before the U.S. Patent and Trademark Office are known by Appellants to have any substantive relationship to the subject matter of this Appeal.

STATUS OF CLAIMS

Claims 1-43 and 47-52, all of the claims in the Application, have been finally rejected under 35 USC 112, first paragraph..

STATUS OF AMENDMENTS

An Amendment to the claims after Final Rejection under 37 CFR 1.116 was filed with the US Patent and Trademark Office on July 25, 2003. There was a substantive amendment to only a single claim (Claim 32) to correct a typographic/editorial error noted by the Examiner and otherwise improve the claim language by correcting internal claim reference and antecedent basis, without adding substantive information. Calls to the PTO have been unable to determine the status of the amendment. It will be assumed that the amendments have been entered in this Appeal.

Additionally, the numbering of the last group of claims 47-52 was changed because of a previous numbering error.

SUMMARY OF THE INVENTION

A method indicates viability of transplanted progenitor or stem cells grown in a culture. This is important, as it gives an indication of how the medical implantation is proceeding and whether any intervention in the procedure is needed. (Page 4, lines 9-28; page 5, lines 22-29). The method is performed with a medical device that supports at least one sensing function (Page 7, lines 23-31). The method comprises non-destructively observing a region of a patient to where cells (Page 6, lines 9-24) have been transplanted; sensing a property within said region of a patient that is indicative of cell viability or inviability of transplanted progenitor or stem cells grown in a culture (Page 6, line 9 through page 7, line 18); and using data from sensing said property within said region to indicate cell viability from a transplant of progenitor or stem cells grown in a culture within the region (Pages 6-15). (All limitations in this description were also found in the original claims)

ISSUES ON APPEAL

The sole issue on Appeal is whether the specification and claims are in compliance with the requirements of 35 U.S.C. 112, first paragraph. Specifically the issues on Appeal are whether Claims 1-43 and 47-49 have been improperly rejected under 35 USC 112, first paragraph, the basis of the rejection believed to be fairly summarized as asserting as follows:

1) The specification enables practice of the invention for MRI methods only;
2) The specification does not enable a sensing method that detects the viability of implanted stems cells, progenitor cells, or differentiated cells;
3) Therefore the specification does not provide enablement commensurate in scope with the claims.

The specific issues on Appeal are:

1) whether claims are properly rejected under 35 USC 112, first paragraph if there is only disclosure of MRI imaging, and whether there is, in fact disclosure of other imaging techniques that are enabled.
2) Whether the specification provides enablement of any sensing methods that detect the viability of implanted stem cells, progenitor cells or differentiated cells.
3) Ultimately whether the specification provides enablement commensurate in scope with the claims.

GROUPING OF CLAIMS

The following grouping of claims is made in compliance with the requirements of 37 C.F.R. 1.191 for the content of an Appeal Brief. The following grouping of claims is made to expedite this Appeal and narrow issues, and is not intended to waive or limit the right of the Applicants to enforce and defend claims separately, even though they are grouped for convenience in this Appeal.

Claims 1, 3-5, 7, 10, 13, 17, 19-20, 22, 25-43 and 47-52 shall stand or fall with the patentability of Claim 1 under this issue.

Claims 2, 6, 8-9, 11-12, 14-16, 18, 21 and 23-24 shall stand or fall with the patentability of claim 2 which specifically recites that magnetic resonance imaging is used for the non-destructive observation.

ARGUMENTS OF APPELLANTS IN RESPONSE TO THE REJECTIONS

Claims 1-43 and 47-49 have been improperly rejected under 35 USC 112, first paragraph, the basis of the rejection believed to be fairly summarized as asserting as follows:

1) The specification enables practice of the invention for MRI methods only;
2) The specification does not enable a sensing method that detects the viability of implanted stems cells, progenitor cells, or differentiated cells;
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3) Ultimately whether the specification provides enablement commensurate in scope with the claims.

The Rejections Under 35 USC 112, first paragraph

Claims 1, 3-5, 7, 10, 13, 17, 19-20, 22, 25-43 and 47-52 shall stand or fall with the patentability of Claim 1 under this issue.

There are a number of confusing and contradictory implications in the rejection. The indication that the specification is enabling for MRI methods only implies the generic functionality for the use of MRI imaging processes to effect the practice of the invention is enabled. On the other hand, the rejection asserts that the specification does not enable a method that detects the viability of stem cells, progenitor cells, and differentiated cells.

The problem with this rejection is the failure to appreciate that all of the various imaging or non-destructive testing methods described in the specification analyze for effects produced by the cells that are indicative of viability and do not measure 'viability' as a quantitative value itself. This is absolutely clear from the disclosure (under 35 USC 112, second paragraph) and is clearly enabled under 35 USC 112, first paragraph. Note the following specific disclosures:

a) "The invention additionally discloses an imaging system to monitor the metabolic status of the transplanted cells and their assimilation into their tissue transplant environment..." Page 5, lines 27-29;

b) "...the software program may operate in a manner that includes at least some of the following steps:..Measure the response of that field to an imaging technology (e.g., MR, fluoroscopy, sonogram, etc.)...Determine...components of the response that are associated with specific readable components (e.g., taggants or natively responsive components, molecules or atoms...Introduce cells into the field. Identifying at least some readable components introduced to the field by introduction of the cells. Comparing concentrations and/or the change in the range...Observing concentrations of change in the range of presence of readable components. Qualitatively and/or quantitatively determining changes and/or rates of changes and/or locations of changes..." (Page 7, line 20-page 8, line 13).

c) "According to methods of the invention, cell viability may be assessed by monitoring the presence of anisotropic water diffusion. (Page 22, lines 18-20). Furthermore,...cell viability may also be assessed by monitoring the increases in local tissue density by measuring the water proton diffusion in the local tissue. (Page 22, lines 22-26).

d) "In another embodiment of the invention, the viability and functional assimilation of the implanted cells may be assessed by monitoring changes in the resting membrane potential of cells in the cell implant." (Page 23, lines 9-11).

e) "In a further embodiment of the invention, cell viability may also be assessed by measuring changes in electrical impedance in the region of the cell implant." (Page 23, lines 20-24).

f) "In a preferred embodiment of the invention, the development of cells into tissues will alter the inherent cellular luminescence, which is monitored by a local optical probe or camera introduced by an image-guided catheter." (Page 26, lines 4-13).

g) "In a further embodiment of the method of the invention, cell viability may be assessed by measuring changes in local tissue temperature using, as one example, probes introduced by image-guided catheters..." (Page 26, lines 19-23).

h) Pages 12, line 13 – page 14, line 15 describes various methods and mechanisms by which cell viability can be determined.

i) Additionally, the specific contains extensive disclosure or methods of analyzing numerous different local properties that are determined by MRI technology (e.g., Pages 15, line 15 – page 17, line 9; page 17, line 16 – page 18, line 3; page 18, line 19 – page 21, line 1; page 22, line 9 – page 23, line 19; page 24, line 6 – page 26, line 3; page 27, line 6 – page 28, line 8).

It is absolutely clear that specification provides a clear statement of measuring properties that are related to, quantifiable to, or quantitative to the viability of implanted cells in a

patient. Different imaging methods are described and enabled (e.g., MRI, sonogram, fluoroscopy, optical fiber, catheter, etc.), different measuring methods are described and enabled (thermal measurements, electrical methods, etc.), and many different properties that can be measured by MRI are described an enabled. The specification therefore is clearly enabling of both various and numerous methods (and enablement is not limited to only MRI systems). The specification is also clearly enabling of various and numerous different properties that may be the basis of quantitative or qualitative measurement to provide a determination of viability of cell implantation. Applicants have therefore made a clear, extensive and enabling disclosure consistent with the requirements of 35 USC 112, first paragraph with respect to the breadth of the invention as claimed.

The rejection under 35 USC 112, first paragraph states, in effect that:

1) The specification enables practice of the invention for MRI methods only; **This has been clearly contradicted and overwhelmed by the cited portions of the specification where fluoroscopy, sonogram, resistance, optical fiber, thermal measurements and other methods have been disclosed and enabled.**
2) The specification does not enable a sensing method that detects the viability of implanted stems cells, progenitor cells, or differentiated cells; **This assertion has been contradicted and overwhelmed by the cited disclosure wherein specific measurements of specific properties have been specified and enabled to show viability, and both methodology and instrumentality have been described to effect this method.**
3) Therefore the specification does not provide enablement commensurate in scope with the claims. **Not only is this assumption in error based upon the review of the nature and extent of the disclosure, but the basis for**

challenging the disclosure is legally inadequate and insufficient as a matter of law.

With regard to the third argument given directly above, it is to be noted that it is a fundamental requirement of the US PTO to establish and support any rejection based upon 35 USC 112, first paragraph with scientific reasoning and analysis of specific facts as to why a specification is not enablement. For example:

> "A threshold issue is whether the PTO met its burden of proof in calling into question the enablement of appellant's disclosure. This burden required that the PTO advance acceptable reasoning inconsistent with enablement.." *In re Strahilevitz*, (1982 C.C.P.A.) 212 U.S.P.Q. 561.

The rejection has not advanced any scientific reasoning why a process reasonably within the scope of the claims as drafted is not enabled. Rather, the specification merely says MRI is enabled, but that "...methods of indicting viability of 'implanted cells, progenitor cells, or differentiated cells' [have]...very limited guidance within the specification as to how this is accomplished. The claimed methods (referring to the broadest claim) require a 'sensing' function of cells within a region of a patient." Contrary to the subsequent misappropriation of language attempting to limit the application to MRI, the quoted language and portions of the specification cited above clearly provides enablement to one skilled in the art that is commensurate with the scope of the claims. The sensing can be focused to specific areas, as is well known with medical imaging techniques of the type enabled in the specification for observation of an area of the patient to sense a property that is indicative of cell viability or inviability. It must be remembered that the legal issue of enablement is to be viewed in the light of one ordinarily skilled in the art.

> "Claims are addressed to the person of average skill in the particular art. Compliance with 112 must be adjudged from that perspective, not in a vacuum. It is always possible to theorize some combination of

> circumstances which would render a claimed composition or method inoperative, but the art-skilled would assuredly not choose such a combination. (*Ex parte Cole, Howarth and Reading*, (PTO Bd. Of Pat. Int. and App.) 233 USPQ 94.

Viewed from the legally required perspective, it is clear both that the PTO has not met even a threshold burden of establishing a *prima facie* case of lack of enablement, and has not given appropriate value to the scope and detail of the specification with respect to the breadth of the invention as viewed and understood by one ordinarily skilled in the art. The rejection is clearly in error and must be withdrawn.

Claims 2, 6, 8-9, 11-12, 14-16, 18, 21 and 23-24 shall stand or fall with the patentability of claim 2 which specifically recites that magnetic resonance imaging is used for the non-destructive observation.

It is also to be noted that some of the claims that have been rejected as lacking enablement recite MRI specifically as the method of imaging (claim 2 and every claim dependent therefore), and that other claims dependent therefrom recite specific methods used, specific properties used, and other limiting characteristics that are clearly enabled by the specification. The rejection is therefore completely inappropriate to such claims, such as, but not limited to, claims 2, 6, 8-9, 11-12, 14-16, 18, 21 and 23-24.

Claim 2 specifically recites that the non-destructive observation is done with magnetic resonance imaging, which the Examiner specifically admits is enabled:

> "...the specification, **while enabling for an MRI method**, does not reasonably provide enabling for a sensing method that detect the viability of implanted stem cells, progenitor cells, or differentiated cells." (Office Action mailed September 10, 2002.

Again, the issue is not whether there is enablement for direct detection of viability (as implied by the rejection), which is not a term ever used in the claims. Rather, the claims (e.g., claim 1, from which claim 2 is dependent), recites:

> "..**sensing a property** within said region of a patient that is **indicative of cell viability or inviability** of transplanted progenitor or stem cells grown in a culture..." (emphasis added)

The rejection therefore asserts that the specification does not enable a limitation that is not found in the claims. That means that the rejection is clearly in error and must be reversed. The specification, as noted above in the discussion of the patentability and enablement of claim 1, clearly identifies specific properties that are indicative of cell viability, clearly identifies multiple methods by which those properties can be non-destructively observed, and fully enables one of ordinary skill in the medical imaging arts to practice the full scope of the claimed invention without undue experimentation.

Of additional importance is the fact that the rejection of record has failed to meet the minimal requirement of shifting the burden of proof on the issue to the Appellant. There is no scientific reasoning, scientific explanation, or substantive theory as to why the specification fails to enable practice of any element or scope of the invention as claimed. As the Rejection of Record has failed to meet even this minimal legal requirement, the rejection must be reversed as a matter of law.

Again in the September 10, 2003 Office Action (on page 3, lines 7-19), the Office Action effectively admits enablement by the MRI method. The type of cell observed is limited in the claims for strategic reasons. The fact that all cells can be tagged, marked, or observed for specific metabolic changes, which to some extent all cells undergo in changing from viability to inviability, and that the rejection acknowledges enablement for detection of metabolic changes such as observing GABA, PCr, creatine, choline, and lactate metabolites, and that the specification enables observation of these metabolic

changes on a molecular scale, evidences enablement of observation of "sensing a property within said region of a patient that is indicative of cell viability or inviability." Because the observation is extremely local, rather then merely taking general blood samples, the observation is also local in its implications. By observing the region of the implantation, the deviation from or compliance with expected observed conditions (which are fully enabled), indicates viability or inviability. This is true generically (with respect to claim 1 etc.) and specifically with respect to MRI imaging (claim 2 etc.).

The rejection is clearly in error and must be reversed.

CONCLUSION

All rejections of record have been shown in detail to be in error. The rejection should be reversed and all claims should be indicated as allowable.

Applicants believe the claims are in condition for allowance and request reconsideration of the application and allowance of the claims. The Examiner is invited to telephone the below-signed attorney at 952-832-9090 to discuss any questions that may remain with respect to the present application.

Respectfully submitted,
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Date September 25, 2003 By 
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I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to MAIL STOP: APPEAL BRIEF-PATENTS, P.O. Box 1450, Commissioner for Patents, Alexandria, VA 22313-1450 on **September 25, 2003**.

Name: Mark A. Litman 
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APPENDIX - THE CLAIMS ON APPEAL

1. (PREVIOUSLY AMENDED) A method for indicating viability of transplanted progenitor or stem cells grown in a culture, the method being performed with a medical device that supports at least one sensing function, the method comprising:

non-destructively observing a region of a patient to where progenitor or stem cells grown in a culture cells have been transplanted;

sensing a property within said region of a patient that is indicative of cell viability or inviability of transplanted progenitor or stem cells grown in a culture; and

using data from sensing said property within said region to indicate cell viability from a transplant of progenitor or stem cells grown in a culture within the region.

2. (ORIGINAL) The method of claim 1 wherein said non-destructively observing comprises magnetic resonance imaging.

3. (ORIGINAL) The method of claim 1 wherein the medical device is guided to said region of a patient using non-destructive observation.

4. (ORIGINAL) The method of claim 1 wherein said medical device is positioned within said region of a patient using non-destructive observation to assist in the positioning.

5. (PREVIOUSLY AMENDED) The method of claim 1 wherein said cell viability is indicated by a property resulting from an event selected from the group consisting of cell activity, cell inactivity, cell growth, cell death, specific cell function, specific cell dysfunction, volumetric expansion of cell population, and volumetric decrease of cell population.

6. (PREVIOUSLY AMENDED) The method of claim 2 wherein said cell viability is indicated by a property resulting from an event selected from the group consisting of cell activity, cell inactivity, cell growth, cell death, specific cell function, specific cell dysfunction, volumetric expansion of cell population, and volumetric decrease of cell population.

7. (PREVIOUSLY AMENDED) The method of claim 1 wherein said property is monitored by observation of at least one parameter selected from the group consisting of local lactate levels, local glucose turnover, local phosphorous high-energy metabolite concentrations, local F-19 labeled metabolites, alterations in tissue sodium, and changes in the conversion rates of O_2 gas to H_2O water.

8. (PREVIOUSLY AMENDED) The method of claim 2 wherein said property is monitored by observation of at least one parameter selected from the group consisting of local lactate levels, local glucose turnover, local phosphorous high-energy metabolite concentrations, local F-19 labeled metabolites, alterations in tissue sodium, and changes in the conversion rates of O_2 gas to H_2O water.

9. (PREVIOUSLY AMENDED) The method of claim 6 wherein said property is monitored by observation of at least one parameter selected from the group consisting of local lactate levels, local glucose turnover, local phosphorous high-energy metabolite concentrations, local F-19 labeled metabolites, alterations in tissue sodium, and changes in the conversion rates of O_2 gas to H_2O water.

10.(ORIGINAL) The method of claim 1 wherein said property is monitored by at least one technique selected from the group consisting of proton spectroscopy, monitoring of

C-13 labeled glucose, monitoring by P-31 MR spectroscopy, monitoring of local F-19 labeled metabolites, monitoring of Na-23 levels, and monitoring of $17O_2$ gas conversion to H_217O water.

11. (ORIGINAL) The method of claim 2 wherein said property is monitored by at least one technique selected from the group consisting of proton spectroscopy, monitoring of C-13 labeled glucose, monitoring by P-31 MR spectroscopy, monitoring of local F-19 labeled metabolites, monitoring of Na-23 levels, and monitoring of $17O_2$ gas conversion to H_217O water.

12. (ORIGINAL) The method of claim 6 wherein said property is monitored by at least one technique selected from the group consisting of proton spectroscopy, monitoring of C-13 labeled glucose, monitoring by P-31 MR spectroscopy, monitoring of local F-19 labeled metabolites, monitoring of Na-23 levels, and monitoring of $17O_2$ gas conversion to H_217O water.

13. (ORIGINAL) The method of claim 1 wherein said medical device includes at least one element selected from the group consisting of a volume coil surrounding the tissue and a local multi-tuned MRI RF coil.

14. (ORIGINAL) The method of claim 2 wherein said medical device includes at least one element selected from the group consisting of a volume coil surrounding the tissue and a local multi-tuned MRI RF coil.

15. (ORIGINAL) The method of claim 9 wherein said medical device includes at least

one element selected from the group consisting of a volume coil surrounding the tissue and a local multi-tuned MRI RF coil.

16. (ORIGINAL) The method of claim 12 wherein said medical device includes at least one element selected from the group consisting of a volume coil surrounding the tissue and a local multi-tuned MRI RF coil.

17. (ORIGINAL) The method of claim 1 wherein said property comprises blood flow or changes in blood flow as vascular supply is developed.

18. (ORIGINAL) The method of claim 2 wherein said property comprises blood flow or changes in blood flow as vascular supply is developed.

19. (ORIGINAL) The method of claim 7 wherein said property comprises blood flow or changes in blood flow as vascular supply is developed.

20. (ORIGINAL) The method of claim 17 wherein blood flow or changes in blood flow are measured by observation of at least one material selected from the group consisting of labeled H_2O water, contrast-agent infusion of TI-shortening agents or T2*-shortening agents, local introduction of hyperpolarized Xenon gas, or optically-active coloring agents.

21. (ORIGINAL) The method of claim 18 wherein blood flow or changes in blood flow are measured by observation of at least one material selected from the group consisting of labeled H_2O water, contrast-agent infusion of TI-shortening agents or T2*-shortening agents, local introduction of hyperpolarized Xenon gas, or optically-active coloring

agents.

22. (ORIGINAL) The method of claim 19 wherein blood flow or changes in blood flow are measured by observation of at least one material selected from the group consisting of labeled H_2O water, contrast-agent infusion of TI-shortening agents or T2*-shortening agents, local introduction of hyperpolarized Xenon gas, or optically-active coloring agents.

23. (ORIGINAL) The method of claim 2 wherein said property comprises anisotropic water diffusion.

24. (ORIGINAL) The method of claim 2 wherein said property comprises the local concentrations of at least one of choline, NAA, GABA, phosphocholine, and creatine.

25. (ORIGINAL) The method of claim 1 wherein the property is selected from the group consisting of a) local tissue density and cell populations, b) local electrical activity, c) local oxygenated/deoxygenated hemoglobin and changes in the local T2* reflecting the alterations in tissue oxygenation, d) changes in the vascular reserve and response to oxygenation stresses, e) tissue fluorescence and bioluminescence, f) tissue fluorescence and bioluminescence, g) electrical impedance, and h) local tissue temperature.

26. (ORIGINAL) The method of claim 1 wherein the property is selected from the group consisting of a) local tissue density and cell populations, b) local electrical activity, c) local oxygenated/deoxygenated hemoglobin and changes in the local T2* reflecting the alterations in tissue oxygenation, d) changes in the vascular reserve and response to oxygenation stresses, e) tissue fluorescence and bioluminescence, f) tissue fluorescence

and bioluminescence, g) electrical impedance, and h) local tissue temperature.

27. (ORIGINAL) A method for indicating viability of transplanted progenitor or stem cells grown in a culture, said method being performed with a medical device that supports at least one sensing function comprising:

non-destructively observing a region of a patient to where progenitor or stem cells grown in a culture have been transplanted;

sensing a property within said region of a patient that is indicative of cell metabolism;

repeating or continuing said sensing of a property over a period of time in which said property changes; and

using data from sensing changes in said property within said region to indicate cell viability from a transplant of progenitor or stem cells grown in a culture within the region.

28. (ORIGINAL) The method of claim 27 wherein said data from sensing changes in said property indicates active metabolic function in transplanted cells.

29. (PREVIOUSLY ADDED) The method of claim 28 wherein changes in said property are monitored by at least one technique selected from the group consisting of proton spectroscopy, monitoring of C-13 labeled glucose, monitoring by P-31 MR spectroscopy, monitoring of local F-19 labeled metabolites, monitoring of Na-23 levels, and monitoring of $17O_2$ gas conversion to H_217O water.

30. (PREVIOUSLY ADDED) A method for indicating viability of transplanted transfected cells, the method being performed with a medical device that supports at least

one sensing function, the method comprising:

non-destructively observing a region of a patient to where transfected cells have been transplanted;

sensing a property within said region of a patient that is indicative of cell viability or inviability of transplanted, transfected cells; and

using data from sensing said property within said region to indicate cell viability from a transplant transfected cells within the region.

31. (PREVIOUSLY ADDED) The method of claim 31 wherein the transfected cells are grown in a culture prior to transplanting.

32. (CURRENTLY AMENDED) A method for indicating viability of transplanted, transfected cells, said method being performed with a medical device that supports at least one sensing function comprising:

non-destructively observing a region of a patient to where transfected cells grown in a culture have been transplanted;

sensing a property within said region of a patient that is indicative of cell metabolism;

repeating or continuing said sensing of a property over a period of time in which said property changes; and

using data from sensing changes in said property within said region to indicate cell viability from a ~~transplantof~~ transplant of transfected cells grown in a culture within the region.

33. (PREVIOUSLY ADDED) A method for indicating viability of transplanted cells implanted into tissue, the method being performed with a medical device that supports at

least one sensing function, the method comprising:

non-destructively observing a region of a patient to where cells have been implanted into tissue;

sensing a property within said region of a patient that is indicative of cell viability or inviability of cells implanted into tissue; and

using data from sensing said property within said region to indicate cell viability from within the region.

34. (PREVIOUSLY ADDED) A method for indicating viability of an implanted colony of cells, the method being performed with a medical device that supports at least one sensing function, the method comprising:

non-destructively observing a region of a patient to where a colony of cells have been implanted;

sensing a property within said region of a patient that is indicative of cell viability or inviability of the implanted colony of cells; and

using data from sensing said property within said region to indicate cell viability from the implanted colony of cells within the region.

35. (PREVIOUSLY ADDED) The method of claim 34 wherein the colony of cells comprise transfected cells.

36. (PREVIOUSLY ADDED) The method of claim 35 wherein the colony of transfected cells have been cultured prior to being implanted.

37. (PREVIOUSLY ADDED) The method of claim 34 wherein an image from the sensing is viewed within 5 minutes of sensing.

38. (PREVIOUSLY ADDED) The method of claim 34 wherein an image from sensing is viewed in near real time.

39. (PREVIOUSLY ADDED) The method of claim 35 wherein an image from sensing is viewed in near real time.

40. (PREVIOUSLY ADDED) The method of claim 36 wherein an image from sensing is viewed in near real time.

41. (PREVIOUSLY ADDED) The method of claim 34 wherein the sensing of a property within said region of a patient that is indicative of cell viability or inviability of the implanted colony of cells is used to quantitate the cell viability.

42. (PREVIOUSLY ADDED) The method of claim 35 wherein the sensing of a property within said region of a patient that is indicative of cell viability or inviability of the implanted colony of cells is used to quantitate the cell viability.

43. (PREVIOUSLY ADDED) The method of claim 36 wherein the sensing of a property within said region of a patient that is indicative of cell viability or inviability of the implanted colony of cells is used to quantitate the cell viability.

44. (PREVIOUSLY CANCELLED)

45. (PREVIOUSLY CANCELLED)

46. (PREVIOUSLY CANCELLED)

47. (PREVIOUSLY ADDED) The method of claim 37 wherein the sensing of a property within said region of a patient that is indicative of cell viability or inviability of the implanted colony of cells is used to quantitate the cell viability.

48. (PREVIOUSLY ADDED) The method of claim 39 wherein the sensing of a property within said region of a patient that is indicative of cell viability or inviability of the implanted colony of cells is used to quantitate the cell viability.

49. (PREVIOUSLY ADDED) The method of claim 30 wherein said property within said region of a patient comprises anisotropic water diffusion.

~~49~~ 50. (RENUMBERED) The method of claim 32 wherein the transplanted, transfected cells have been genetically engineered to express a neurotransmitter, an agonist of a neurotransmitter, a precursor of a transmitter that has neurotransmitter activity, derivative of a neurotransmitter that has neurotransmitter activity, analog of a neurotransmitter that has neurotransmitter activity, or fragment of a neurotransmitter that has neurotransmitter activity.

~~50~~ 51. (RENUMBERED) The method of claim 32 wherein the transplanted cells have been genetically engineered to express a neurotransmitter, an agonist of a neurotransmitter, a precursor of a transmitter that has neurotransmitter activity, derivative of a neurotransmitter that has neurotransmitter activity, analog of a neurotransmitter that has neurotransmitter activity, or fragment of a neurotransmitter that has neurotransmitter activity.

~~51~~ 52. (RENUMBERED) The method of claim 32 wherein the implanted colony of cells comprise cells that have been genetically engineered to express a neurotransmitter, an agonist of a neurotransmitter, a precursor of a transmitter that has neurotransmitter activity, derivative of a neurotransmitter that has neurotransmitter activity, analog of a neurotransmitter that has neurotransmitter activity, or fragment of a neurotransmitter that has neurotransmitter activity.

~~52~~ 53. (RENUMBERED) The method of claim 32 wherein the transplanted progenitor or stem cells have been genetically engineered to express a neurotransmitter, an agonist of a neurotransmitter, a precursor of a transmitter that has neurotransmitter activity, derivative of a neurotransmitter that has neurotransmitter activity, analog of a neurotransmitter that has neurotransmitter activity, or fragment of a neurotransmitter that has neurotransmitter activity.